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STURM & FIX LLP
206 SIXTH AVENUE
SUITE 1213
DES MOINES, IA 50309-4076

EXAMINER
MAIER, LEIGH C

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/091,917	Applicant(s) Lis
	Examiner Leigh Maier	Art Unit 1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-9 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-9 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

Claims 1-9 are pending.

Claim Objections

Claims 4, 8, and 9 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the terms "preferably" and "more preferably" render the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Further regarding claim 1, the claim recites the limitation of "high compressibility." The term "high" is a relative term which renders the claim indefinite. This term is not defined by the claim, the specification does not provide an objective standard for ascertaining the requisite degree of compressibility, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Regarding claim 5, the claim recites a limitation of a "compressibility of greater than 70 N expressed in a C test." However, from a reading of the specification, it appears that this measurement is dependent on the exact conditions used during the test. See page 5, second paragraph of the instant specification. From the search, it does not appear that a "C test" is a method that is commonly used in this art, or that it necessarily *defines* the conditions used. Furthermore, the lower table on page 7 indicates that this measurement is the "hardness." This variability in terminology and testing methods renders the claims vague and indefinite.

Beta-cyclodextrins are physically characterized in a number of ways in the prior art. MUNOZ-RUIZ (J. Pharm. Pharmacol., 1996) reports the "compressibility" of several cyclodextrins as a percentage. See Table 2. SALEH (J. Pharm. Belg., 1993) reports "hardness" vs. compression force, but this does not appear to correspond to the instant "hardness" measurement, because of the different units of measure. See Figure 3. This reference also reports "tensile strength," but again, this does not appear to be quite the same measurement. See Table II. The closest type of measurement in the art appears to be what GIORDANO (Int., J. Pharm., 1990) calls "crushing strength" as it appears to depend on the size and density of the tablet and is

measured in units of force. See page 154, third paragraph and Figure 1. The reference further states that "crushing strength was adopted as the parameter for evaluating the compaction capacity." See page 154, first paragraph.

For the reasons set forth above, one of ordinary skill would not reasonably be apprised of the metes and bounds of the claims.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, and 7 rejected under 35 U.S.C. 102(b) as being anticipated by PANDE et al (Int., J. Pharm., 1995).

PANDE teaches the preparation of highly compactible BCD by dehydration under various conditions followed by rehydration. See all of page 233, and Tables 1 and 2. The disclosed BCDs have size fractions of greater than 80 μm. See page 233, section 2.3.3. The reference further teaches that the water content is critical and that this stays essentially stable at a relative humidity of 52%. See Table 3 and text in the same column. This is comparable to the storage at 54% relative humidity for testing in the instant specification. The reference does not make a

determination of "compressibility" in a manner that can be easily compared with the limitations of the claims. However, the products are prepared in the manner of the instant invention, thus resulting in the same physical properties.

Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Claims 1 and 5-7 rejected under 35 U.S.C. 102(b) as being anticipated by GIORDANO et al (Int., J. Pharm., 1990).

GIORDANO discloses BCD having a mean diameter of 146 μm. See page 154, second paragraph. The "crushing strength" (a measurement that appears to correspond to "compressibility" as discussed above) of a variety of BCDs is reported, and this measurement is a function of the water content of the the BCD. See Figure 1. These crushing strength range from 15 N to 300 N. It is noted that these tests are done under different conditions, so that they are not strictly comparable. However, the reference goes on to state that a BCD having a water content of 14.5% that was first *de*hydrated and then *re*hydrated was more than twice that of a BCD with a comparable water content that had not undergone this dehydration step. BCDs prepared in the same manner as in the instant invention, would be presumed to have the same physical

characteristics as those of the invention. With regard to the "stability" of the products, this is an inherent physical characteristic. At the optimum conditions, (the claim does not limit the conditions regarding relative humidity, etc.) these products, prepared as in the instant invention should remain stable.

Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Finally, Applicant admits that products existed that meet the limitations of the claims at the time the invention was made. See Example 5 of the instant specification: Comparison with *prior art* products. One of these is a Nihon product, which appears to be the same as that used by GIORDANO.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over PANDE et al (Int., J. Pharm., 1995).

The claims are drawn to a BCD having a compressibility of greater than 70 N in a C test. Dependent claim 6 recites a specific surface area of greater than or equal to 1 m^2/g for a designated particle size fraction.

PANDE teaches as set forth above. The reference teaches that the specific surface area of the product depends on the conditions of pretreatment, i.e. temperature: pretreatment at a higher temperature gives a product with a greater specific surface area, and a product with a higher specific surface area is more compressible (holding constant for water content). From the data in Table 2, it would appear that a particle size fraction as recited in the claim would not have the required specific surface area. However, there are fractions that are very close, up to 0.92 m^2/g.

It would have been obvious to one having ordinary skill in the art to pretreat the BCD at a higher temperature in order to prepare a product with a higher surface area. It is the object of PANDE to prepare a highly compactible product for direct compression tabletting. Therefore, it would have been obvious to optimize the result effective variables, temperature of pretreatment, water content, and relative humidity of storage environment, through routine experimentation. In doing so, one of ordinary skill would be reasonably expected success in preparing a product having the specific surface area recited in the claims.

Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over PANDE et al (Int., J. Pharm., 1995) as applied to claims 1, 5, and 7 above, and further in view of GABEL et al (US 6,294,196).

The claims are drawn to a process for preparing a highly compressible BCD comprising dehydrating and rehydrating a starting BCD. Dependents are drawn to the use of a fluidized air bed granulator for the dehydration and/or the rehydration.

PANDE teaches as set forth above. The reference is silent regarding the use of a fluidized air bed granulator.

GABEL teaches the use of a fluidized bed granulator (Aeromatic type) in the preparation of pharmaceutical excipients. See col 7-9. The reference describes material being hydrated and dried in a manner in the art.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use a fluidized bed granulator to accomplish the process that was taught by PANDE. One of ordinary skill would be motivated to use such an apparatus for scaling up the process for mass production. It would be within the scope of the artisan to select an apparatus that is known in the art to have utility in processing pharmaceutical excipients.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Monday-Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier
Patent Examiner
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